A Continuous Molecular Roadmap to iPSC Reprogramming through Progression Analysis of Single-Cell Mass Cytometry.

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Public Summary:

Scientific Abstract:
To analyze cellular reprogramming at the single-cell level, mass cytometry was used to simultaneously measure markers of pluripotency, differentiation, cell-cycle status, and cellular signaling throughout the reprogramming process. Time-resolved progression analysis of the resulting data sets was used to construct a continuous molecular roadmap for three independent reprogramming systems. Although these systems varied substantially in Oct4, Sox2, Klf4, and c-Myc stoichiometry, they presented a common set of reprogramming landmarks. Early in the reprogramming process, Oct4(high)Klf4(high) cells transitioned to a CD73(high)CD104(high)CD54(low) partially reprogrammed state. Ki67(low) cells from this intermediate population reverted to a MEF-like phenotype, but Ki67(high) cells advanced through the M-E-T and then bifurcated into two distinct populations: an ESC-like Nanog(high)Sox2(high)CD54(high) population and a mesendoderm-like Nanog(low)Sox2(low)Lin28(high)CD24(high)PDGFR-alpha(high) population. The methods developed here for time-resolved, single-cell progression analysis may be used for the study of additional complex and dynamic systems, such as cancer progression and embryonic development.